AMENDMENTS

In the claims:

Pursuant to 37 C.F.R. §1.121 the following is a complete listing of the claims of the present application:

1. (original) A method of regulating endothelial cell growth, comprising the step of contacting endothelial cells with a composition comprising a purified polypeptide in an amount effective to regulate endothelial cell growth, wherein said polypeptide:

(a) binds the extracellular domain of Flt4 receptor tyrosine kinase and stimulates Flt4 autophosphorylation;

(b) has an apparent molecular weight of about 23 kD as assessed by SDS-PAGE under reducing conditions; and

(c) has an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit binding to the Flt4 extracellular domain.

2. (original) A method according to claim 1, wherein amino terminal amino acids 2 through 18 of said polypeptide have an amino acid sequence corresponding to amino acids 2 through 18 set forth in SEQ ID NO: 5.

3. (original) A method according to claim 1, wherein said polypeptide is purifyable from conditioned media from a PC-3 prostatic adenocarcinoma cell line, said cell line having ATCC CRL No. 1435, using an affinity purification procedure wherein the affinity purification matrix comprises a polypeptide comprising the extracellular domain of Flt4 receptor tyrosine kinase.

4. (original) A method according to claim 1 wherein the endothelial cells are lymphatic endothelial cells.

5. (currently amended) A method of modulating the activity of Flt4 receptor tyrosine kinase (Flt4), comprising ~~the steps of:~~

~~identifying a patient in need of modulation of Flt4 activity; and~~

administering to ~~the~~ a patient a composition comprising a purified polypeptide in an amount effective to modulate the activity of Flt4, wherein the polypeptide binds the extracellular domain (EC) of Flt4 and stimulates Flt4

phosphorylation in mammalian cells expressing Flt4, said polypeptide comprising an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit such binding.

6. (canceled)

7. (currently amended) A method according to claim 5, 8, or 41 wherein the composition further comprises a pharmaceutically-acceptable diluent, adjuvant, or carrier.

8. (currently amended) A method according to claim 5, ~~wherein the identifying step comprises~~ comprising identifying a patient suffering from a disorder of the lymphatic system, ~~and~~ wherein the polypeptide is administered in an amount effective to modulate Flt4 activity in endothelial cells of lymphatic vessels of the patient.

9. (currently amended) A method according to claim ~~5~~ 8, wherein the polypeptide binds Flt4 and promotes proliferation of lymphatic endothelial cells that express Flt4.

10. (canceled)

11. (original) A method according to claim 5, wherein the polypeptide comprises a contiguous portion of SEQ ID NO: 8 that is sufficient to bind human Flt4EC,

wherein said contiguous portion includes eight cysteine residues that are conserved in human vascular endothelial growth factor (VEGF), human platelet derived growth factor A (PDGF-A), and human platelet derived growth factor B (PDGF-B), and

wherein said polypeptide lacks any portion of SEQ ID NO: 8 that has one or more cysteine motifs of a Balbiani ring 3 protein (BR3P).

12. (original) A method according to claim 5, wherein the polypeptide comprises a portion of the amino acid sequence in SEQ ID NO: 8 effective to permit said binding to the Flt4 extracellular domain, said polypeptide lacking at least carboxy-terminal residues of SEQ ID NO: 8 beyond residue 227.

13. (original) A method according to claim 5, wherein the polypeptide is purifiable from conditioned media from a PC-3 prostatic adenocarcinoma cell line, said cell line having ATCC Accession Number CRL 1435, using an affinity purification procedure wherein the affinity purification matrix comprises a polypeptide comprising the extracellular domain of Flt4 receptor tyrosine kinase.

14. (original) A method according to claim 5, wherein the polypeptide has an amino acid sequence consisting of a portion of the amino acid sequence set forth in SEQ ID NO: 8, said portion including from residue 161 of SEQ ID NO: 8 to residue 211 of SEQ ID NO: 8, said portion lacking at least carboxy-terminal residues of SEQ ID NO: 8 beyond residue 227.

15. (original) A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes from residue 131 of SEQ ID NO: 8 to residue 211 of SEQ ID NO: 8.

16. (original) A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes from residue 113 of SEQ ID NO: 8 to residue 213 of SEQ ID NO: 8.

17. (original) A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes amino acids 103 to 217 of SEQ ID NO: 8.

18. (original) A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes amino acids 32 to 227 of SEQ ID NO: 8.

19. - 27. (canceled)

28. (previously presented) A method of stimulating the proliferation of mammalian endothelial cells comprising the step of contacting mammalian endothelial cells with a composition comprising a polypeptide in an amount effective to modulate the proliferation of mammalian endothelial cells, said polypeptide comprising a VEGF-C ΔC156 polypeptide that binds to human Flt4 receptor tyrosine kinase (Flt4) and fails to bind to human KDR receptor tyrosine (VEGFR-2), said

polypeptide having an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit binding to Flt4, wherein the cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid.

29. (original) A method according to claim 28, wherein the portion of SEQ ID NO: 8 is selected from the group consisting of:

(a) a continuous portion having as its amino terminal residue an amino acid between residues 102 and 114 of SEQ ID NO: 8 and having as its carboxy terminal residue an amino acid between residues 212 and 228 of SEQ ID NO: 8, wherein the cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid;

(b) continuous portions that comprise an amino-terminal truncation of (a); and

(c) continuous portions that comprise a carboxyl-terminal truncation of (a) or (b).

30. (original) A method according to claim 28, wherein said endothelial cells are lymphatic endothelial cells.

31. (previously presented) An in vivo method according to claim 28, wherein the contacting step comprises administering to a mammalian subject in need of stimulation of the growth of lymphatic endothelial cells a composition comprising said polypeptide, in an amount effective to stimulate the growth of lymphatic endothelial cells in vivo.

32. (original) A method according to claim 31, wherein said polypeptide has reduced effect on the permeability of mammalian blood vessels compared to a wildtype VEGF-C polypeptide with an amino acid sequence set forth in SEQ ID NO: 8 from residue 103 to residue 227.

33. (previously presented) A method of stimulating the proliferation of mammalian endothelial cells comprising the step of contacting mammalian endothelial cells with a composition comprising a polypeptide in an amount effective to stimulate the proliferation of mammalian endothelial cells, said polypeptide comprising a fragment of a vertebrate prepro-VEGF-amino acid sequence that binds to human Flt4 receptor tyrosine kinase, with the proviso that, in said polypeptide, a

conserved cysteine of the vertebrate prepro-VEGF-C has been deleted or replaced by another amino acid,

wherein the vertebrate prepro-VEGF-C amino acid sequence comprises an amino acid sequence that is encoded by a DNA of vertebrate origin which hybridizes to a non-coding strand complementary to nucleotides 352 to 1611 of SEQ ID NO: 7 under the following hybridization conditions: hybridization at 42°C in a hybridization solution comprising 50% formamide, 5 X SSC, 20 mM Na•PO4, pH 6.8; and washing in 0.2 X SSC at 55°C,

wherein nucleotides 352 to 1611 of SEQ ID NO: 7 encode a human prepro-VEGF-C having the amino acid sequence set forth in SEQ ID NO: 8 that is characterized by eight cysteine residues at positions 131, 156, 162, 165, 166, 173, 209, and 211 of SEQ ID NO: 8 that are conserved in human vascular endothelial growth factor (VEGF), human platelet derived growth factors A and B (PDGF-A, PDGF-B), human placenta growth factor (PlGF-1), and human vascular endothelial growth factor B (VEGF- B), and

wherein the conserved cysteine that has been deleted or replaced corresponds to position 156 of SEQ ID NO: 8.

34. (original) A method according to claim 33, wherein the vertebrate is a human.

35. (original) A method according to claim 33, wherein the vertebrate is a mouse.

36. (original) A method according to claim 33, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 8, wherein the cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid;

(b) the amino acid sequence of SEQ ID NO: 11, wherein the cysteine residue at position 152 of SEQ ID NO: 11 has been deleted or replaced by another amino acid;

(c) the amino acid sequence of SEQ ID NO: 13, wherein the cysteine residue at position 155 of SEQ ID NO: 13 has been deleted or replaced by another amino acid;

(d) amino-terminal truncations of (a), (b), or (c); and

(e) carboxyl-terminal truncations of (a), (b), (c), or (d).

37. (previously presented) An in vivo method according to claim 33, wherein the contacting step comprises administering to a mammalian subject in need of stimulation of the growth of lymphatic endothelial cells a composition comprising said polypeptide, in an amount effective to modulate the growth of lymphatic endothelial cells in vivo.

38. (canceled)

39. (canceled)

40. (previously presented) A method according to claim 19, further comprising a step of purifying the secreted polypeptide prior to the contacting step.

41. (new) A method according to claim 5, comprising identifying a patient in need of modulation of myelopoiesis, wherein the polypeptide is administered in an amount effective to modulate myelopoiesis.